CASE REPORTS

Refer to: Laiken S, Beck CH Jr, Timms RM: Acute renal failure associated with hemodialysis and hypophosphatemia. West J Med 128:343-345, Apr 1978

Acute Renal Failure Associated With Hemodialysis and Hypophosphatemia

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IN RECENT YEARS the significance of hypophosphatemia has been increasingly recognized.[1,2] Several authors have noted a hemolytic anemia produced by hypophosphatemia.[3,4] Here, a case will be described in which hemolysis occurred during hemodialysis for salicylate overdose and led to acute renal failure in a patient subsequently found to be severely hypophosphatemic.

Report of a Case

The patient was a 50-year-old white man who arrived in the emergency room comatose after transfer from another hospital where the diagnosis of salicylate intoxication was made. After speaking with the patient's family it was learned that he suffered from a poorly defined low back pain and had been ingesting increasing doses of aspirin over the 48 hours before admission. Although it was not known at the time of admission it was subsequently found that he also had been consuming daily an estimated two quarts of magnesium aluminum hydroxide containing antacid, for known peptic ulcer disease. Initial and follow-up history indicated that he had not been exposed to heavy metals or other nephrotoxins.

On physical examination the patient was obtunded and appeared older than his stated age. Blood pressure was 150/100 mm of mercury, heart rate was 90 beats per minute with regular rhythm and there were 25 deep respirations per minute. Jugular venous pressure was normal by inspection. The chest was clear and results of cardiac and abdominal examinations were unremarkable. Neurological evaluation showed cranial nerves 2 through 12 to be intact. The deep tendon reflexes were normal and bilaterally symmetrical. There was no Babinski sign. The patient reacted to painful stimuli and was able to move all extremities. He was unable to follow most simple commands, could not sit up and was unaware of the presence of others.

Laboratory studies gave the following values: salicylate level, 90 mg per dl; serum sodium, 150 mEq per liter; chloride, 115 mEq per liter; potassium, 3.5 mEq per liter; bicarbonate, 17 mEq per liter; blood urea nitrogen, 20 mg per dl; creatinine, 1.3 mg per dl; albumin, 3.8 grams per dl, and serum glucose, 136 mg per dl. Arterial blood gas studies showed an oxygen pressure of 89 mm of mercury, a carbon dioxide pressure of 16 mm of mercury and a pH of 7.39 on room air. Hematocrit was 32 percent; hemoglobin, 10 grams per dl; leukocyte count, 12,100 cells per cu mm; prothrombin time, 13.9 seconds with control of 11.4 seconds; platelets were normal by smear, and the red blood cell indices were hypochromic and microcytic. The patient's stool was positive for occult blood. Toxicology screen was negative except for salicylate.

The patient was initially given 25 mg of vitamin K_1 intramuscularly, an infusion of 5 percent glucose with normal saline, 150 mEq of sodium bicarbonate, and one dose of acetazolamide, 250 mg given intravenously. Because of the patient's high salicylate level and poor clinical status, it was elected to lower the salicylate level by hemodialysis. Silastic catheters were placed in the femoral veins bilaterally by the Seldinger technique. Dialysis was carried out with regional heparinization using a Gambro Lundia Optima 17 cartridge for 3¼ hours with arterial blood flow of 215 ml per minute and dialysate flow of 500 ml per minute. Dialysate conductivity and temperature were within normal limits during the entire dialysis making hyposmolality of the dialysate unlikely. The dialysate from the dialyzer was Clinitest® negative and therefore thought to be formaldehyde free before the patient was treated.

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Submitted, revised, June 27, 1977.

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This treatment reduced the salicylate level to 40 mg per dl. Clear yellow urine was initially excreted at greater than 100 ml per hour. Midway through dialysis the urine abruptly became red brown and decreased in volume to less than 20 ml per hour. During this time there was no significant drop in arterial blood pressure or decrease in weight, and the calculated serum osmolalities before and after dialysis were 293 and 291, respectively. An analysis of urine showed numerous red blood cells, and 4 plus protein. The spun supernatant also was 4 plus for protein and strongly positive for occult blood. The patient's plasma was noted to be pink in color. All blood sent to the laboratory was reported as grossly hemolyzed including a sample with a phosphorus value of 2.3 mg per dl and a calcium level of 8.4 mg per dl. Eight hours after dialysis, the serum free hemoglobin was 125 mg per dl (normal less than 5 mg per dl for this laboratory). Despite a fluid challenge and a transient increase in urine output with 320 mg of intravenous furosemide, the blood urea nitrogen and creatinine values rose to 28 mg per dl and 2.6 mg per dl, respectively, eight hours after dialysis.

The serum phosphorus value 18 hours after the onset of oliguria was 0.4 mg per dl on a nonhemolyzed specimen. At the same time the serum free hemoglobin was 2 mg per dl. The hematocrit had decreased to 24 percent by 24 hours after dialysis. Consequently, a transfusion was then done with 4 units of banked packed red blood cells. The patient's blood urea nitrogen and creatinine values increased and the oliguria persisted for six days. Treatment was carried out with potassium hydrogen phosphate solution, raising the serum phosphorus level to 3.9 mg per dl. Thereafter, hemodialysis was carried out without complication. After a week the patient entered the diuretic phase of acute renal failure. Hemoglobin casts were noted in the urine. Within several weeks the blood urea nitrogen and creatinine values returned to normal. A glucose-6-phosphate dehydrogenase (G6PD) screen was obtained and showed the presence of enzyme. The P_{50} (partial pressure of oxygen at which hemoglobin is 50 percent saturated) was 21 mm of mercury before phosphate repletion and 48 hours after transfusion.

Discussion

The patient described here clearly underwent a hemolytic episode during hemodialysis. This produced acute hemoglobinuria and renal failure. To our knowledge such episodes have not been encountered with hemodialytic therapy for aspirin intoxication in the past. No such problem has been reported related to acetazolamide and bicarbonate therapy for salicylate poisoning.[5] A hemolytic reaction to one dose of acetazolamide seems unlikely because the drug will cause a pancytopenia rarely, but not hemolysis.[6] In addition, acute hemolysis secondary to sulfonamides evolves over a considerably longer time and is usually accompanied by a leukemoid reaction.[7,8] In this patient hemolysis occurred within four hours and the leukocyte count actually decreased to less than 10,000.

It appears likely that the hemolysis was secondary to hypophosphatemia. The initial result with a phosphorus value of 2.3 mg per dl on a grossly hemolyzed specimen is undoubtedly an overestimate, because hemolysis is known to falsely elevate the serum phosphorus value.[9] This is substantiated by the low serum phosphorus value (0.4 mg per dl) after hemolysis ceased. The clearance of phosphate with the dialyzer used is only 58 ml per minute for the given arterial and dialysate flows.[10] If this patient had a normal serum phosphorus before dialysis he would not have had sufficient dialyzer clearance capability or length of dialysis to lower the serum phosphorus to this level.[16] Alkalosis, especially respiratory alkalosis, is thought to be a cause of severe hypophosphatemia.[11] However, this patient was not alkalotic during the time covered by this report. Increasing the serum phosphorus to the normal range allowed subsequent dialysis without hemolysis.

The hypophosphatemia seen in this man was most likely due to chronic aluminum-magnesium hydroxide antacid abuse. This drug has been used experimentally to produce a phosphate depletion syndrome in human volunteers.[1] It is thought that the hemolytic anemia of hypophosphatemia is a result of increasing erythrocyte fragility with adenosine triphosphate depletion.[3] One would expect fragile erythrocytes to be particularly susceptible to hemolysis when subjected to passage through a hemodialyzer.

In addition to excessive antacid consumption, hypophosphatemia is known to occur in a variety of clinical situations, including acute and chronic alcoholism, sepsis and hyperalimentation with phosphate-poor solutions.[9] While a direct cause-effect relationship between hypophosphatemia

and hemolysis in relation to hemodialysis is not proven by this report, the circumstantial evidence is compelling. It seems prudent to obtain a serum phosphate value before hemodialysis of patients in whom hypophosphatemia is clinically suspected. Patients with severe hypophosphatemia could be readily treated in the hope of preventing hemolysis.

Patients with hypophosphatemia may be depleted of red cell 2,3 diphosphoglycerate.[12] Oxyhemoglobin dissociation was notably abnormal in this patient with a large leftward shift in the oxyhemoglobin dissociation curve. The abnormal P_{50} may have been caused by the severe hypophosphatemia aggravated by the transfusions with banked red cells probably already low in red cell 2,3 diphosphoglycerate. With hemolysis resulting in a sudden loss of hemoglobin, the combination of anemia and increased affinity of hemoglobin for oxygen could acutely threaten tissue oxygenation. This is further reason for recognition and early treatment of hypophosphatemia.

Summary

The clinical importance of hypophosphatemia has become increasingly recognized. A case of hemoglobinuric renal failure following hemodialysis of a severely hypophosphatemic patient is described. It is proposed that the increased erythrocyte fragility of hypophosphatemic patients may predispose them to hemolysis during hemodialysis and the importance of correcting serum phosphate concentration in such patients is stressed.

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Refer to: Daskalakis MK: Fibromuscular hyperplasia of external iliac arteries. West J Med 128:345-347, Apr 1978

Fibromuscular Hyperplasia of External Iliac Arteries

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FIBROMUSCULAR HYPERPLASIA of the external iliac arteries may represent a part of the whole involvement of the arterial system or may represent a localized manifestation of the disease. Symptoms of the arterial insufficiency and clinical findings are related to the degree of stenosis, and impairment of blood flow. The purpose of this communication is to report such a symptomatic case and to review the surgical procedures which have been used for the management of patients with fibromuscular hyperplasia of external iliac arteries. To our knowledge, surgical approach with dilatation of the external iliac arteries has not previously been reported in patients with fibromuscular hyperplasia.

Report of a Case

A 52-year-old white man was admitted to West Anaheim Community Hospital on January 30, 1973, with a four-year history of intermittent claudication of both lower extremities. Physical examination gave the following findings: blood pressure, 140/85 mm of mercury; systolic bruit over both iliac arteries with radiation to both femoral arteries; notably diminished femoral, popliteal, posterior tibial arterial pulses and absent pedis dorsalis pulses bilaterally.

An aortogram showed typical changes of fibromuscular hyperplasia of external iliac arteries bilaterally (Figure 1). Surgical operation was carried out on February 7, 1973, under general anesthesia and dilatation of the iliac arteries, bilaterally, was done through bilateral groin incision and transverse arteriotomies of common femoral arteries. Bakes dilators, sizes 3 to 9 mm, were used progressively with some resistance en-

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Submitted June 2, 1977.

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